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RESPONSE AFTER FINAL REJECTION
EXPEDITED PROCEDURE
EXAMINING GROUP 1630

PATENT
Customer No. 22,852
Attorney Docket No. 02481.1742

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)

E. UHLMANN et al.)

Application No.: 09/835,370)

Group Art Unit: 1637

Filed: April 17, 2001)

Examiner: SIEW

For: POLYAMIDE NUCLEIC ACID)
DERIVATIVES AND AGENTS AND)
PROCESSES FOR PREPARING THEM)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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REQUEST FOR RECONSIDERATION AFTER FINAL REJECTION

Sir:

This paper is being filed in response to the Final Office Action dated October 30, 2003.

Applicants respectfully request reconsideration and withdrawal of the rejections set forth in the Final Office Action in view of the following remarks. Claims 1-85 are pending in this application, only claims 1-15, 20-23, and 31-85 having been examined on the merits in the Office Action.

I. *Drawings*

The Office states that the courtesy drawings filed August 14, 2003, are not in the PTO file, and requests that Applicants re-submit them. (Final Office Action at paragraph 3.) Attached

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to this Request is a copy of the 12 sheets of drawings (12 figures) submitted with the application on April 17, 2001, and re-submitted on August 14, 2003. Also attached is a copy of a stamped postcard, indicating that the 12 sheets of drawings were filed by Applicants, and received by the Office, with the application on April 17, 2001, and again on August 14, 2003. Because the attached papers were timely filed in complete form, Applicants believe that no petition or fee is due for re-submission of them. However, if any petition or fee is required, please grant the petition and charge the fee to our Deposit Account No. 06-0916.

II. *Restriction Requirement*

The Office reasserts the finality of the Restriction Requirement. (Final Office Action at paragraph 4.) Applicants respectfully request that, because the claims of elected Group I are related to those of non-elected Groups II and III as a product and process of using and making, in accordance with MPEP § 821.04, the non-elected process claims of Groups II and III be rejoined with the product claims of Group I once one or more product claims are found to be allowable.

III. *Rejections Under 35 U.S.C. § 102*

A. Uhlmann et al.

The Office maintains the rejection of claims 1-9, 20, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by Uhlmann et al. (*Nucleosides and Nucleotides*, 1997). (Final Office Action at paragraph 5.) The Office finds the Applicants' response unpersuasive where the Applicants differentiated the presently claimed compounds from those of *Uhlmann* by pointing

out that, among other things, *Uhlmann* does not disclose a compound possessing a phosphoryl radical at the N-terminus. In this regard, the Office asserts that the limitations of the claims do not necessarily require a phosphoryl radical, but rather Q may also be hydroxyl or an amino acid derivative which, according to the Office, reads broadly on *Uhlmann*. Applicants respectfully traverse this rejection.

The present claims are directed to PNA derivatives of a given formula, Formula I, in which Q is a hydroxyl, amino, NHR_7 , HR_7R_8 , an amino acid derivative, or a peptide radical. See present claim 1. Thus, the Office is correct when it states that "Q may be hydroxyl or any amino acid derivative." However, Applicants submit that this basis for maintaining the rejection is improper because the moiety represented by "Q" is at the C-terminus of the compound represented by Formula I, not the N-terminus. As such, the Office's position, that the possible moieties represented by "Q" in claim 1 may be hydroxyl or an amino acid derivative, does not support its stated conclusion.¹

In view of the fact that "Q" in claim 1 is at the C-terminus, not the N-terminus, of the compound recited in present claim 1, Applicants submit that their previous arguments should have been sufficient to differentiate the presently claimed compounds from those of *Uhlmann*. Accordingly, Applicants request that the Office reconsider those arguments, and withdraw the outstanding rejection of claims 1-9, 20, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by *Uhlmann*.

¹ The Office's attention is directed to pages 31-33, paragraphs 63-65, for a description of preparation of compounds according to the present invention by extension of the N-terminus of a PNA compound.

B. Breipohl et al.

The Office maintains the rejection of claims 1-12, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by Breipohl *et al.* (U.S. Patent No. 6,046,306). (Final Office Action at paragraph 6.) The Office asserts that *Breipohl* anticipates the present claims because, in the present claims, "Q may be hydroxyl or any amino acid derivative". Applicants respectfully traverse this rejection.

As discussed above, the present claims are directed to PNA derivatives of a given formula, Formula I, in which Q is a hydroxyl, amino, NHR_7 , HR_7R_8 , an amino acid derivative, or a peptide radical. Thus, the Office is correct when it states that "Q may be hydroxyl or any amino acid derivative". However, Applicants submit that this basis for maintaining the rejection is improper because the moiety represented by "Q" is at the C-terminus of the compound represented by Formula I, not the N-terminus. Because "Q" of claim 1 is at the C-terminus of the compound, not the N-terminus, the Office's position does not support its stated conclusion.

In view of the fact that "Q" in claim 1 is at the C-terminus, not the N-terminus, of the compound recited in present claim 1, Applicants submit that their previous arguments should have been sufficient to differentiate the presently claimed compounds from those of *Breipohl*. Accordingly, Applicants request that the Office reconsider those arguments, and withdraw the outstanding rejection of claims 1-12, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by *Breipohl*.

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IV. *Rejections Under 35 U.S.C. § 103*

A. *Uhlmann et al.* in view of *Weiler et al.*

The Office maintains the rejection of claims 22 and 23 under 35 U.S.C. § 103(a) as unpatentable over *Uhlmann et al.* in view of *Weiler et al.* (Nucl. Acids Res. 1997). (Final Office Action at paragraph 7.) The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-aminoethyl)glycine units, and *Weiler* for the teaching of construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Uhlmann's* PNAs. Applicants respectfully submit that, regardless of whether or not it would be obvious to try to use *Uhlmann's* PNAs in *Weiler's* arrays, the combination of *Uhlmann* and *Weiler* does not render present claims 22 and 23 obvious.

Claims 22 and 23 depend from claim 1. Thus, if the PNA derivative of claim 1 is not disclosed or suggested by the combination of *Uhlmann* and *Weiler*, then claims 22 and 23 cannot be obvious either.

For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claims 22 and 23 obvious, *Weiler* must at least disclose or suggest the PNA derivative of claim 1, in addition to teaching the use of such a PNA derivative in microarrays. Applicants submit that *Weiler* does not teach either of these.

Weiler describes the synthesis of macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not disclose or suggest the PNA derivative of present claim 1.

Furthermore, *Weiler* is limited to macroarrays, whereas present claim 22 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the microarrays of claim 23 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays).

This same argument was made in the previous response; however, the Office did not respond to it. Applicants request that, in response to this paper, the Office respond to this aspect of their arguments.

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA derivatives carrying one or more phosphoryl radicals at their N-termini.

For at least these reasons, Applicants submit that the combination of *Uhlmann* and *Weiler* fails to render present claims 22 and 23 obvious. Accordingly, Applicants submit that present claims 22 and 23 are patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Weiler*.

B. Breipohl *et al.* in view of Weiler *et al.*

The Office maintains the rejection of claims 22 and 23 under 35 U.S.C. § 103(a) as unpatentable over Breipohl *et al.* in view of Weiler *et al.* (Final Office Action at paragraph 8.) The Office relies on *Breipohl* to teach labelled polyamide nucleic acids, and *Weiler* to teach construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Breipohl's* PNAs. Applicants respectfully submit that, regardless of

whether or not it would be obvious to try to use *Breipohl's* PNAs in *Weiler's* arrays, the combination of *Breipohl* and *Weiler* does not render present claims 22 and 23 obvious.

As discussed above, to render claims 22 and 23 obvious, the combination of *Breipohl* and *Weiler* must disclose or suggest the PNA derivative of present claim 1. For the reasons discussed above, Applicants submit that *Breipohl* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claims 22 and 23 obvious, *Weiler* must at least disclose or suggest the PNA derivative of present claim 1, in addition to teaching the use of such a PNA derivative in microarrays. Applicants submit that *Weiler* does not teach either of these.

Weiler describes the synthesis of a macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not disclose or suggest the PNA derivative of present claim 1.

Furthermore, as discussed above, *Weiler* is limited to macroarrays, whereas present claim 22 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the microarrays of claim 22 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays). This same argument was made in the previous response; however, the Office did not respond to it. Applicants request that, in response to this paper, the Office respond to this aspect of their arguments.

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA derivatives carrying one or more phosphoryl radicals at their N-termini.

For at least these reasons, Applicants submit that the combination of *Breipohl* and *Weiler* fails to render present claims 22 and 23 obvious. Accordingly, Applicants submit that present claims 22 and 23 are patentable under 35 U.S.C. § 103(a) over the combination of *Breipohl* and *Weiler*.

C. Uhlmann *et al.* in view of Manoharan *et al.*

The Office maintains the rejection of claims 13-15 under 35 U.S.C. § 103(a) as unpatentable over Uhlmann *et al.* in view of Manoharan *et al.* (U.S. Patent No. 6,043,352). (Final Office Action at paragraph 9.) The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-aminoethyl)glycine units, and *Manoharan* for the teaching of use of PNAs, and in particular PNAs specific for the HA ras translation start site, in pharmaceutical compositions. The Office then concludes that it would have been obvious to make a pharmaceutical composition comprising a PNA according to *Uhlmann* that is specific for the HA ras translation start site, as taught by *Manoharan*. Applicants respectfully submit that, regardless of whether or not it would be obvious to try to use *Uhlmann's* PNAs in *Manoharan's* pharmaceutical compositions, the combination of *Uhlmann* and *Manoharan* does not render present claims 13-15 obvious.

Claims 13-15 depend from claim 1. Thus, to render claims 13-15 obvious, *Uhlmann* or *Manoharan* must disclose or suggest the PNA derivative of claim 1. For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest a PNA derivative according to claim 1. Thus, in order for the combination of *Uhlmann* and *Manoharan* to render claims 13-15 obvious, *Manoharan* must disclose or suggest at least a PNA derivative according to claim 1.

Applicants submit that *Manoharan* does not disclose or suggest such a PNA derivative. The Office has not identified any such teaching, and Applicants have found no such teachings in *Manoharan*.

Because the combination of *Uhlmann* and *Manoharan* fails to disclose or suggest the PNA derivatives of present claim 1, the combination fails to render the PNA derivatives of present claim 1 obvious. Accordingly, the combination of *Uhlmann* and *Manoharan* cannot render the PNA derivatives of claims 13-15 obvious. For at least this reason, Applicants submit that claims 13-15 are patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Manoharan*. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 13-15 under 35 U.S.C. § 103(a) as unpatentable over *Uhlmann* in view of *Manoharan*.

V. *Conclusion*

Applicants submit that present claims 1-15, 20-23, and 31-85 are neither anticipated nor rendered obvious by the cited references. Therefore, Applicants request that the Office withdraw the outstanding rejections, rejoin method claims 16-19 and 24-30, and permit this application to issue as a U.S. patent in due course. If the Office believes anything further is necessary in order to place this application in even better condition for allowance, Applicants request that their undersigned representative be contacted at the telephone number or e-mail address below to discuss the remaining issues.

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Please grant any extension of time required to enter this response and charge any required fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Attachment:
Re-submission of Figures 1-12

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